

WHAT IS CLAIMED IS:

1. A method of screening for modulators of C-reactive protein comprising:

obtaining a C-reactive protein;
contacting the C-reactive protein with at least a first candidate substance;
5 assaying for an interaction between the C-reactive protein and the first candidate
substance with an assay.
2. The method of claim 1, wherein the assay comprises assaying for C-reactive
protein induction of the expression of an adhesion molecule.
- 10 3. The method of claim 2, wherein the adhesion molecule is ICAM-1, VCAM, or E-
selectin.
4. The method of claim 2, wherein the first candidate substance inhibits C-reactive
protein induced expression of the adhesion molecule.
5. The method of claim 2, wherein the first candidate substance enhances C-reactive
15 protein induced expression of the adhesion molecule.
6. The method of claim 1, wherein the assay comprises assaying for C-reactive
protein induction of the expression of a receptor, signaling molecule, cytokine, adhesion
molecule, or an enzyme.
7. The method of claim 6, wherein the cytokine is a chemokine.
- 20 8. The method of claim 7, wherein the chemokine is MCP-1.
9. The method of claim 7, wherein the first candidate substance inhibits C-reactive
protein induced expression of the chemokine molecule.
10. The method of claim 7, wherein the first candidate substance enhances C-reactive
protein induced expression of the chemokine molecule.

11. The method of claim 1, wherein the assay comprises assaying for iNOS induction, receptor for advanced glycation endproducts, monocyte chemoattractant protein-1, P-selectin, endothelin-1, endothelin-receptor, interleukin-6 or heme oxygenase-1.
12. The method of claim 1, wherein obtaining C-reactive protein comprises
5 expressing C-reactive protein in a transgenic cell or an animal.
13. The method of claim 12, wherein the C-reactive protein is expressed in the cell before contacting the C-reactive protein with a first candidate substance.
14. The method of claim 1, wherein obtaining C-reactive protein comprises procuring an expressed C-reactive protein.
- 10 15. The method of claim 14, wherein the C-reactive protein is procured by isolation from a cell.
16. The method of claim 15, wherein the cell comprises a recombinant nucleic acid sequence encoding a C-reactive protein and the C-reactive protein is expressed from the recombinant nucleic acid sequence.
- 15 17. The method of claim 14, wherein the C-reactive protein is isolated from serum.
18. The method of claim 17, wherein the serum is human serum.
19. The method of claim 1, wherein contacting the C-reactive protein with a first candidate substance comprises incubating a cell in a composition comprising C-reactive protein.
- 20 20. The method of claim 19, wherein the cell is incubated with C-reactive protein and serum.
21. The method of claim 20, wherein the serum is human serum.
22. The method of claim 19, wherein the cell is a human cell.

23. The method of claim 22, wherein the cell is a human umbilical vein endothelial cell.
24. The method of claim 19, wherein the cell is comprised in an animal.
25. The method of claim 24, wherein the animal is a human.
- 5 26. The method of claim 24, wherein the C-reactive protein is injected into the animal.
27. The method of claim 24, wherein the first candidate substance is injected into the animal.
- 10 28. The method of claim 1, wherein the first candidate substance is comprised in serum.
29. The method of claim 28, wherein the serum is human serum.
30. The method of claim 28, wherein the first candidate substance is admixed with serum prior to contacting the C-reactive protein with the first candidate substance.
- 15 31. The method of claim 28, wherein the first candidate substance is contained in naturally occurring serum.
32. The method of claim 1, wherein the identity of the first candidate substance is known prior to performance of the screening method.
33. The method of claim 1, wherein the identity of the first candidate substance is unknown prior to performance of the screening method.
- 20 34. The method of claim 33, wherein the first candidate substance is comprised in a mixture of possible candidate substances.
35. The method of claim 33, further comprising determining the identity of the first candidate substance after the performance of the screening method.

36. The method of claim 33, further comprising isolating the first candidate substance after the performance of the screening method.

37. The method of claim 33, further comprising determining characteristics of the first candidate substance after the performance of the screening method.

5 / 38. A method of inhibiting C-reactive protein modulated inflammation comprising:

obtaining a modulator of C-reactive protein identified by a method comprising:

obtaining a C-reactive protein;

contacting the C-reactive protein with at least a first candidate substance;

assaying for an interaction between the C-reactive protein and the first candidate

10 substance with an assay;

incorporating the modulator of C-reactive protein in a pharmaceutically

acceptable carrier to form a pharmaceutical composition;

and administering the pharmaceutical composition to a subject.

15 39. The method of claim 38, wherein the modulator inhibits the development of cardiovascular complications.

40. The method of claim 39, wherein the modulator is given to a subject with angina.

41. The method of claim 39, wherein the modulator is given to a subject with myocardial infarction.

20 42. The method of claim 39, wherein the modulator is given to subject who is at risk of atherosclerosis or ischemic heart disease.

43. The method of claim 42, wherein the modulator is given to the subject in a prophylactic manner.

25 44. The method of claim 39, wherein the modulator is given to a subject with myocardial infarction.

45. The method of claim 38, wherein the modulator inhibits the development of a stroke.
46. The method of claim 38, wherein the modulator inhibits the development inflammatory disease, wherein the inflammatory disease is enhanced by C-reactive protein.
47. The method of claim 38, wherein the modulator is given in a single dose.
48. The method of claim 38, wherein the modulator is given in a series of doses.
49. The method of claim 48, wherein the modulator is given in daily doses.
50. A modulator of C-reactive protein produced by a method comprising:
obtaining a C-reactive protein;
contacting the C-reactive protein with a candidate substance;
assaying for an interaction between the C-reactive protein and the candidate substance;
determining that the candidate substance is a modulator of C-reactive protein.
51. The modulator of claim 50, wherein the modulator is comprised in a pharmaceutically acceptable carrier.
52. A method of screening for a modified modulator, wherein a first candidate substance is isolated comprising:
obtaining a C-reactive protein;
contacting the C-reactive protein with the first candidate substance;
assaying for an interaction between the C-reactive protein and the first candidate substance to establish a baseline of a non-modified modulator;
modifying the first candidate substance;
contacting C-reactive protein with the modified first candidate substance; and

assaying for an interaction between the modified modulator in the presence of C-reactive protein and comparing the modified modulator interaction with the established baseline of the non-modified modulator.

- 5 53. The method of claim 52, wherein modifying the first candidate substance comprises modification of the amino acid or nucleic acid sequence of the first candidate substance.
54. The method of claim 52, wherein the modified nucleic acid sequence is inserted into an expression vector.
- 10 55. The method of claim 54, wherein the expression vector comprises a reporter molecule.
56. The method of claim 55, wherein the expression vector is transfected into cells.
57. The method of claim 56, wherein the cells are embryonic stem cells.
58. The method of claim 57, wherein transfected embryonic stem cells are implanted
15 into a blastocyst to produce a transgenic mouse.
59. The method of claim 53, wherein the modified nucleic acid sequence is injected into the embryo to produce a transgenic animal.
60. The method of claim 53, wherein the first candidate substance is a receptor, signaling molecule, cytokine, adhesion molecule or an enzyme.
- 20 61. The method of claim 56, further comprising measuring the reporter molecule after transfection.
62. The method of claim 61, wherein measuring the reporter molecule comprises protein expression, protein activity or binding activity.